



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 12-093/S-043
NDA 12-940/S-043

JUN 16 1999

Wyeth Laboratories
Attention: Ms. Roberta R. Acchione
170 North Radnor-Chester Road
St. Davids, PA 19087-5221

Dear Ms. Acchione:

Please refer to your supplemental new drug applications dated April 7, 1999 (received April 9, 1999) and April 8, 1999 (received April 12, 1999), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Isordil (isosorbide dinitrate) Sublingual Tablets (NDA 12-940) and Oral Tablets (12-093), respectively.

These supplemental new drug applications provide for final printed labeling revised by adding the following bolded text as the first warning under the **WARNING** section:

Amplification of the vasodilatory effects of Isordil by sildenafil can result in severe hypotension. The time course and dose dependence of this interaction have not been studied. Appropriate supportive care has not been studied, but it seems reasonable to treat this as a nitrate overdose, with elevation of the extremities and with central volume expansion.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling included in the April 7 and 8, 1999 submissions. Accordingly, these supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Gary Buehler
Regulatory Health Project Manager
(301) 594-5300

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
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